
Identification and Generation of Long Term Repopulating Human Muscle Stem Cells from Human Pluripotent Stem Cells

Grant Award Details

Identification and Generation of Long Term Repopulating Human Muscle Stem Cells from Human Pluripotent Stem Cells

Grant Type: Quest - Discovery Stage Research Projects

Grant Number: DISC2-10695

Investigator:

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|---------------------|---------------------------------------|
| Name: | April Pyle |
| Institution: | University of California, Los Angeles |
| Type: | PI |

Disease Focus: Muscular Dystrophy

Award Value: \$2,184,000

Status: Pre-Active

Grant Application Details

Application Title: Identification and Generation of Long Term Repopulating Human Muscle Stem Cells from Human Pluripotent Stem Cells

Public Abstract:**Research Objective**

We will molecularly and functionally define muscle stem cells in human muscle in development, juvenile and adult and develop strategies to generate the most regenerative muscle stem cells from hPSCs.

Impact

There is no clinically relevant cell endowed with continuous repopulation ability from hPSCs. This work could provide a cell therapy for muscle disorders including muscular dystrophies or sarcopenia.

Major Proposed Activities

- We will perform single cell RNA sequencing (scRNA-seq) of embryonic, fetal, juvenile and adult muscle stem cells (MuSCs) and identify unique gene signatures and cell states across human myogenesis.
- We will identify unique cell surface markers on in vivo derived MuSCs that distinguish PAX7-positive cells from other muscle cells and across cell states.
- Evaluate myogenic ability and functional differences of embryonic, fetal, juvenile and adult MuSCs in fusion, proliferation, engraftment and repopulation assays in mouse models of muscle disease.
- Develop transcription factor over-expression in combination with improved directed differentiation strategies to generate MuSCs from hPSCs with genetic and functional signatures of the in vivo MuSCs.
- Demonstrate ability to expand optimal MuSC population from hPSCs for 3-6 passages using novel small molecules without loss of engraftment and repopulation potential in mouse models of muscle disease.
- Identification of one translational candidate MuSC population from hPSCs capable of continuous repopulation after injury.

Statement of Benefit to California:

A large majority of California residents are affected or will be affected with a muscle disease in their lifetime including severe muscular dystrophies, aging related muscle loss called sarcopenia or muscle weakness. The research in this proposal will benefit CA residents tremendously by understanding how to generate a muscle stem cell capable of responding to injury and undergoing long term repopulation after injury to generate new muscle. Funding will also support additional staff in the lab.

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